REMARKS

Allowed claims 2, 4, 8 and 9 have been amended to make grammatical corrections. In addition, allowed claims 4, 5, 8 and 9 have been amended to remove dependency from other claims, *i e.* to be placed in independent form. New claims 18-26 are added as independent claims derived from allowed claim 10. New claim 27 is added as a multiple dependent claim to recite the use of compounds from allowed claim 3 in the methods of claims 4, 5, 8, 9 or 18-26 inclusive. Support for these amendments and additions is found throughout the specification and claims as filed, for example, page 25, lines 17-27; page 29, line 10 – page 36, line 27; page 41, lines 5-14; the Examples; and claims 5, and 8-10 as filed. No new matter has been added.

Applicant submits that the foregoing claim amendments are formal in nature and do not require substantive examination by the Examiner. Accordingly, Applicant respectfully requests that this Amendment be entered. For the Examiner's convenience, a copy of the allowed claims together with the claims presented in the instant amendment is attached hereto as Appendix A.

Please charge the amount of $1,152.00 to our Deposit Account No. 12-0080 to cover the fee for the additional claims presented by the instant amendment. Also, please charge any other necessary fees due to our Deposit Account No. 12-0080.

Respectfully submitted,

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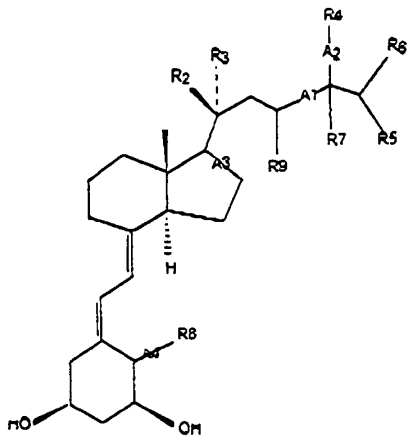
Date: August 17, 1999

APPENDIX A

2. An isolated 3-epi form of a 1α-hydroxy-vitamin D3 compound having formula II as follows:

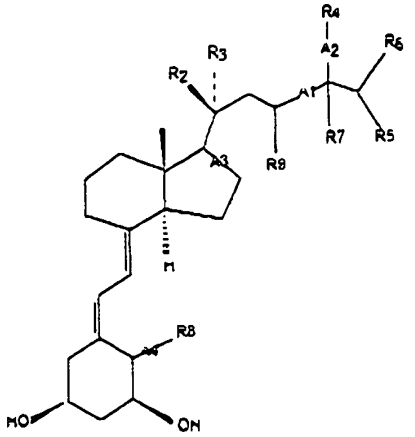


II

wherein A_1 is a single, a double, or a triple bond; A_2, A_3 and A4 are each independently selected from the group consisting of a single or a double bond; R_2, R_3, R_4, R_7, R_8 and R_9 are independently selected from the group consisting of a hydrogen, a deuterium, a deuteroalkyl, a hydroxy, an alkyl, an alkoxide, an O-acyl, a halogen, a haloalkyl, a hydroxyalkyl, an amine or a thiol group, and wherein the pairs of R_2 and R_3, and R_4 and R_7 taken together are an oxygen atom; and R_5 and R_6 are independently selected from the group consisting of a hydrogen, a deuterium, a halogen, an alkyl, a hydroxyalkyl, a haloalkyl, and a deuteroalkyl.

3. The compound of claim 2, which is 1α(OH) vitamin D3, 1α,24 dihydroxy 3-epi vitamin D_3, 1α hydroxy 24-ethyl 3-epi vitamin D_3, 1α hydroxy 24-methyl 3-epi vitamin D_3, or 1α, 24-dihydroxy 24-methyl 3-epi vitamin D_3.

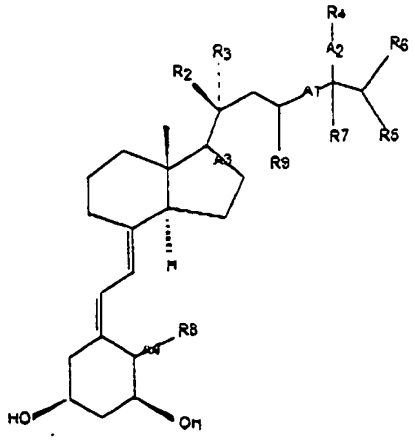
4. A method of treating a disorder characterized by an aberrant activity of a vitamin D_3-responsive cell, comprising administering to a subject an effective amount of a vitamin D_3 compound having formula II as follows:



II

wherein A_1 is a single, a double, or a triple bond; A_2, A_3 and A4 are each independently selected from the group consisting of a single or a double bond; R_2, R_3, R_4, R_7, R_8 and R_9 are independently selected from the group consisting of a hydrogen, a deuterium, a deuteroalkyl, a hydroxy, an alkyl, an alkoxide, an O-acyl, a halogen, a haloalkyl, a hydroxyalkyl, an amine or a thiol group, and wherein the pairs of R_2 and R_3, and R_4 and R_7 taken together are an oxygen atom; and R_5 and R_6 are independently selected from the group consisting of a hydrogen, a deuterium, a halogen, an alkyl, a hydroxyalkyl, a haloalkyl, and a deuteroalkyl, such that the aberrant activity of the vitamin D_3-responsive cell is reduced.

5. A method of treating a disorder characterized by an aberrant activity of a hyperproliferative skin cell, comprising administering to a subject an effective amount of an isolated 3-epi form of a 1α-hydroxy-vitamin D3 compound having formula II as follows:



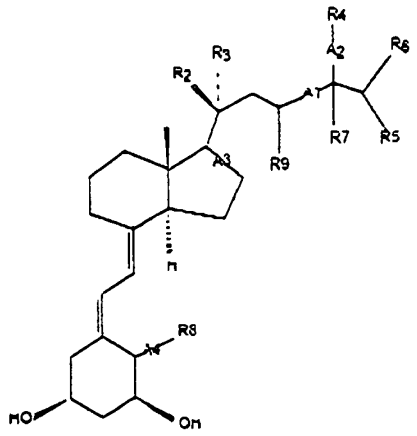
II

wherein A_1 is a single, a double, or a triple bond; A_2, A_3 and A4 are each independently selected from the group consisting of a single or a double bond; R_2, R_3, R_4, R_7, R_8 and R_9 are independently selected from the group consisting of a hydrogen, a deuterium, a deuteroalkyl, a hydroxy, an alkyl, an alkoxide, an O-acyl, a halogen, a haloalkyl, a hydroxyalkyl, an amine or a thiol group, and wherein the pairs of R_2 and R_3, and R_4 and R_7 taken together are an oxygen atom; and R_5 and R_6 are independently selected from the group consisting of a hydrogen, a deuterium, a halogen, an alkyl, a hydroxyalkyl, a haloalkyl, and a deuteroalkyl, such that the aberrant activity of the hyperproliferative skin cell is reduced.

6. The method of claim 4, wherein the disorder comprises an aberrant activity of an endocrine cell.

7. The method of claim 6, wherein the endocrine cell is a parathyroid cell and the aberrant activity is processing and/or secretion of parathyroid hormone.

8. A method of treating secondary hyperparathyroidism, comprising administering to a subject an effective amount of an isolated 3-epi form of a 1α-hydroxy-vitamin D3 compound having formula II as follows:

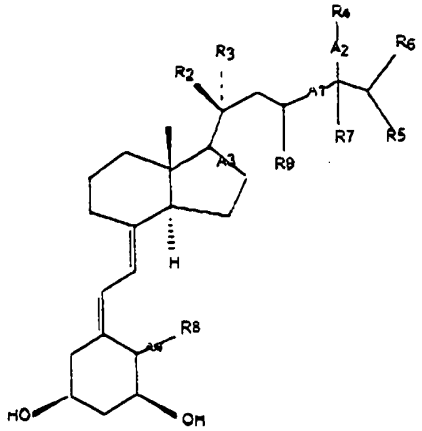


II

wherein A_1 is a single, a double, or a triple bond; A_2, A_3 and A4 are each independently selected from the group consisting of a single or a double bond; R_2, R_3, R_4, R_7, R_8 and R_9 are independently selected from the group consisting of a hydrogen, a deuterium, a deuteroalkyl, a hydroxy, an alkyl, an alkoxide, an O-acyl, a halogen, a haloalkyl, a

hydroxyalkyl, an amine or a thiol group, and wherein the pairs of R_2 and R_3, and R_4 and R_7 taken together are an oxygen atom; and R_5 and R_6 are independently selected from the group consisting of a hydrogen, a deuterium, a halogen, an alkyl, a hydroxyalkyl, a haloalkyl, and a deuteroalkyl.

9. A method of treating a disorder characterized by an aberrant activity of a bone cell, comprising administering to a subject an effective amount of an isolated 3-epi form of a 1α-hydroxy-vitamin D3 compound having formula II as follows:



II

wherein A_1 is a single, a double, or a triple bond; A_2, A_3 and A4 are each independently selected from the group consisting of a single or a double bond; R_2, R_3, R_4, R_7, R_8 and R_9 are independently selected from the group consisting of a hydrogen, a deuterium, a deuteroalkyl, a hydroxy, an alkyl, an alkoxide, an O-acyl, a halogen, a haloalkyl, a hydroxyalkyl, an amine or a thiol group, and wherein the pairs of R_2 and R_3, and R_4 and R_7 taken together are an oxygen atom; and R_5 and R_6 are independently selected from the group consisting of a hydrogen, a deuterium, a halogen, an alkyl, a hydroxyalkyl, a haloalkyl, and a deuteroalkyl, such that the aberrant activity of the bone cell is reduced.

10. The method of claim 9, wherein the disorder is selected from the group consisting of osteoporosis, osteodystrophy, senile osteoporosis, osteomalacia, rickets, osteitis fibrosa cystica, renal osteodystrophy, secondary hyperparathyrodism, cirrhosis, and chronic renal disease.

11. The method of claim 4, wherein the subject is a mammal.

12. The method of claim 11, wherein the mammal is a human.

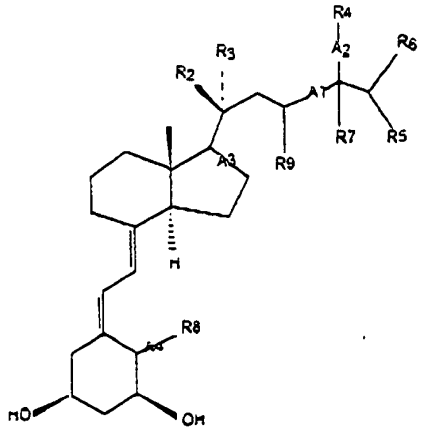
13. A method of ameliorating a deregulation of calcium and phosphate metabolism, comprising administering to a subject a therapeutically effective amount of a 3-epi vitamin D_3 compound of any of claims 2 or 3, so as to ameliorate the deregulation of the calcium and phosphate metabolism.

14. The method of claim 13, wherein the deregulation of the calcium and phosphate metabolism leads to osteoporosis.

15. A pharmaceutical composition comprising, a therapeutically effective amount of a vitamin D_3 compound of claim 2, and a pharmaceutically acceptable carrier.

16. The composition of claim 15, which is suitable for topical or oral administration.

18. A method of treating osteoporosis, comprising administering to a subject an effective amount of an isolated 3-epi form of a 1α-hydroxy-vitamin D3 compound having formula II as follows:

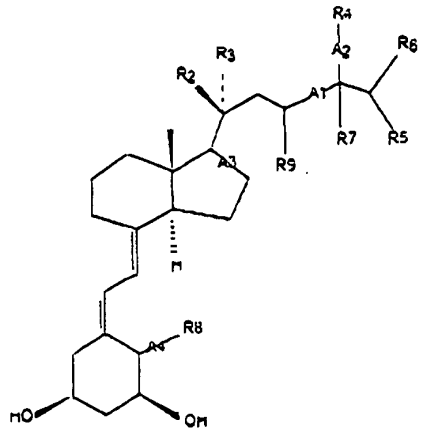


II

wherein A_1 is a single, a double, or a triple bond; A_2, A_3 and A4 are each independently selected from the group consisting of a single or a double bond; R_2, R_3, R_4, R_7, R_8 and R_9 are independently selected from the group consisting of a hydrogen, a deuterium, a deuteroalkyl, a hydroxy, an alkyl, an alkoxide, an O-acyl, a halogen, a haloalkyl, a hydroxyalkyl, an amine or a thiol group, and wherein the pairs of R_2 and R_3, and R_4 and R_7 taken together are an oxygen atom; and R_5 and R_6 are independently selected from

the group consisting of a hydrogen, a deuterium, a halogen, an alkyl, a hydroxyalkyl, a haloalkyl, and a deuteroalkyl.

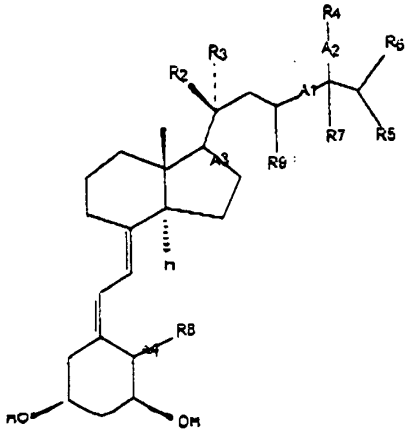
19. A method of treating osteodystrophy, comprising administering to a subject an effective amount of an isolated 3-epi form of a 1α-hydroxy-vitamin D3 compound having formula II as follows:



II

wherein A_1 is a single, a double, or a triple bond; A_2, A_3 and A4 are each independently selected from the group consisting of a single or a double bond; R_2, R_3, R_4, R_7, R_8 and R_9 are independently selected from the group consisting of a hydrogen, a deuterium, a deuteroalkyl, a hydroxy, an alkyl, an alkoxide, an O-acyl, a halogen, a haloalkyl, a hydroxyalkyl, an amine or a thiol group, and wherein the pairs of R_2 and R_3, and R_4 and R_7 taken together are an oxygen atom; and R_5 and R_6 are independently selected from the group consisting of a hydrogen, a deuterium, a halogen, an alkyl, a hydroxyalkyl, a haloalkyl, and a deuteroalkyl.

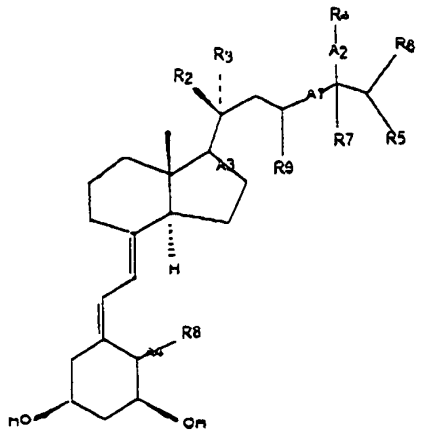
20. A method of treating senile osteoporosis, comprising administering to a subject an effective amount of an isolated 3-epi form of a 1α-hydroxy-vitamin D3 compound having formula II as follows:



II

wherein A_1 is a single, a double, or a triple bond; A_2, A_3 and A4 are each independently selected from the group consisting of a single or a double bond; R_2, R_3, R_4, R_7, R_8 and R_9 are independently selected from the group consisting of a hydrogen, a deuterium, a deuteroalkyl, a hydroxy, an alkyl, an alkoxide, an O-acyl, a halogen, a haloalkyl, a hydroxyalkyl, an amine or a thiol group, and wherein the pairs of R_2 and R_3, and R_4 and R_7 taken together are an oxygen atom; and R_5 and R_6 are independently selected from the group consisting of a hydrogen, a deuterium, a halogen, an alkyl, a hydroxyalkyl, a haloalkyl, and a deuteroalkyl.

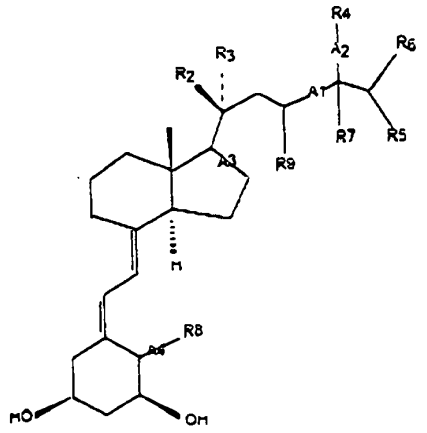
21. A method of treating osteomalacia, comprising administering to a subject an effective amount of an isolated 3-epi form of a 1α-hydroxy-vitamin D3 compound having formula II as follows:



II

wherein A_1 is a single, a double, or a triple bond; A_2, A_3 and A4 are each independently selected from the group consisting of a single or a double bond; R_2, R_3, R_4, R_7, R_8 and R_9 are independently selected from the group consisting of a hydrogen, a deuterium, a deuteroalkyl, a hydroxy, an alkyl, an alkoxide, an O-acyl, a halogen, a haloalkyl, a hydroxyalkyl, an amine or a thiol group, and wherein the pairs of R_2 and R_3, and R_4 and R_7 taken together are an oxygen atom; and R_5 and R_6 are independently selected from the group consisting of a hydrogen, a deuterium, a halogen, an alkyl, a hydroxyalkyl, a haloalkyl, and a deuteroalkyl.

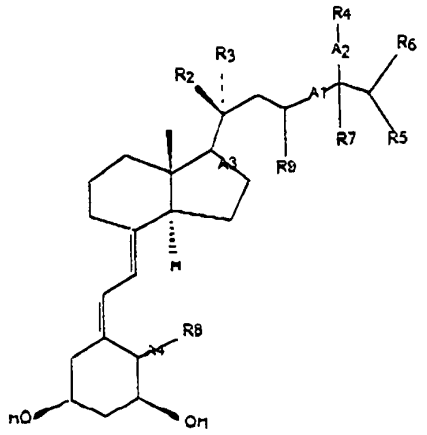
22. A method of treating rickets, comprising administering to a subject an effective amount of an isolated 3-epi form of a 1α-hydroxy-vitamin D3 compound having formula II as follows:



II

wherein A_1 is a single, a double, or a triple bond; A_2, A_3 and A4 are each independently selected from the group consisting of a single or a double bond; R_2, R_3, R_4, R_7, R_8 and R_9 are independently selected from the group consisting of a hydrogen, a deuterium, a deuteroalkyl, a hydroxy, an alkyl, an alkoxide, an O-acyl, a halogen, a haloalkyl, a hydroxyalkyl, an amine or a thiol group, and wherein the pairs of R_2 and R_3, and R_4 and R_7 taken together are an oxygen atom; and R_5 and R_6 are independently selected from the group consisting of a hydrogen, a deuterium, a halogen, an alkyl, a hydroxyalkyl, a haloalkyl, and a deuteroalkyl.

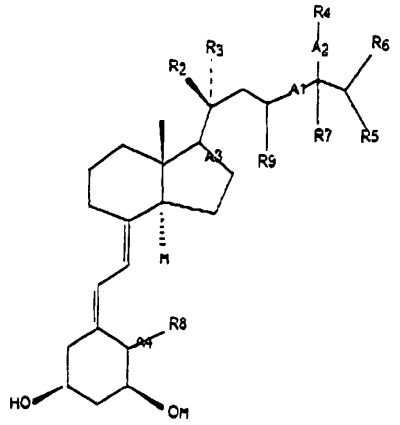
23. A method of treating osteitis fibrosa cystica, comprising administering to a subject an effective amount of an isolated 3-epi form of a 1α-hydroxy-vitamin D3 compound having formula II as follows:



II

wherein A_1 is a single, a double, or a triple bond; A_2, A_3 and A4 are each independently selected from the group consisting of a single or a double bond; R_2, R_3, R_4, R_7, R_8 and R_9 are independently selected from the group consisting of a hydrogen, a deuterium, a deuteroalkyl, a hydroxy, an alkyl, an alkoxide, an O-acyl, a halogen, a haloalkyl, a hydroxyalkyl, an amine or a thiol group, and wherein the pairs of R_2 and R_3, and R_4 and R_7 taken together are an oxygen atom; and R_5 and R_6 are independently selected from the group consisting of a hydrogen, a deuterium, a halogen, an alkyl, a hydroxyalkyl, a haloalkyl, and a deuteroalkyl.

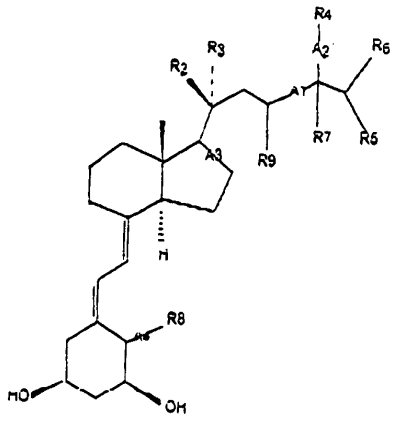
24. A method of treating renal osteodystrophy, comprising administering to a subject an effective amount of an isolated 3-epi form of a 1α-hydroxy-vitamin D3 compound having formula II as follows:



II

wherein A_1 is a single, a double, or a triple bond; A_2, A_3 and A4 are each independently selected from the group consisting of a single or a double bond; R_2, R_3, R_4, R_7, R_8 and R_9 are independently selected from the group consisting of a hydrogen, a deuterium, a deuteroalkyl, a hydroxy, an alkyl, an alkoxide, an O-acyl, a halogen, a haloalkyl, a hydroxyalkyl, an amine or a thiol group, and wherein the pairs of R_2 and R_3, and R_4 and R_7 taken together are an oxygen atom; and R_5 and R_6 are independently selected from the group consisting of a hydrogen, a deuterium, a halogen, an alkyl, a hydroxyalkyl, a haloalkyl, and a deuteroalkyl.

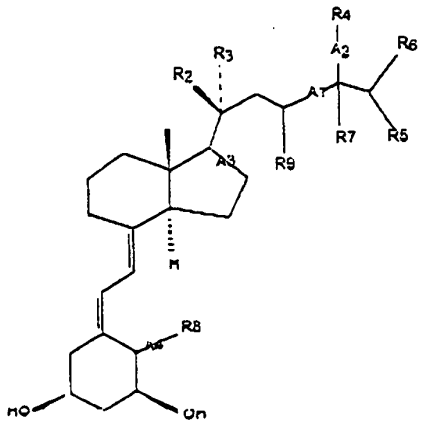
25. A method of treating cirrhosis, comprising administering to a subject an effective amount of an isolated 3-epi form of a 1α-hydroxy-vitamin D3 compound having formula II as follows:



II

wherein A_1 is a single, a double, or a triple bond; A_2, A_3 and A4 are each independently selected from the group consisting of a single or a double bond; R_2, R_3, R_4, R_7, R_8 and R_9 are independently selected from the group consisting of a hydrogen, a deuterium, a deuteroalkyl, a hydroxy, an alkyl, an alkoxide, an O-acyl, a halogen, a haloalkyl, a hydroxyalkyl, an amine or a thiol group, and wherein the pairs of R_2 and R_3, and R_4 and R_7 taken together are an oxygen atom; and R_5 and R_6 are independently selected from the group consisting of a hydrogen, a deuterium, a halogen, an alkyl, a hydroxyalkyl, a haloalkyl, and a deuteroalkyl.

26. A method of treating chronic renal disease, comprising administering to a subject an effective amount of an isolated 3-epi form of a 1α-hydroxy-vitamin D3 compound having formula II as follows:



II

wherein A_1 is a single, a double, or a triple bond; A_2, A_3 and A4 are each independently selected from the group consisting of a single or a double bond; R_2, R_3, R_4, R_7, R_8 and R_9 are independently selected from the group consisting of a hydrogen, a deuterium, a deuteroalkyl, a hydroxy, an alkyl, an alkoxide, an O-acyl, a halogen, a haloalkyl, a hydroxyalkyl, an amine or a thiol group, and wherein the pairs of R_2 and R_3, and R_4 and R_7 taken together are an oxygen atom; and R_5 and R_6 are independently selected from the group consisting of a hydrogen, a deuterium, a halogen, an alkyl, a hydroxyalkyl, a haloalkyl, and a deuteroalkyl.

27. The method of any one of claims 4, 5, 8, 9 or 18-26 inclusive, wherein said compound is 1α(OH) vitamin D3, 1α,24 dihydroxy 3-epi vitamin D_3, 1α hydroxy 24-ethyl 3-epi vitamin D_3, 1α hydroxy 24-methyl 3-epi vitamin D_3, or 1α, 24-dihydroxy 24-methyl 3-epi vitamin D_3.